

**S/N Unknown**

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Margo Haygood et al. Examiner: Unknown  
Serial No.: Unknown Group Art Unit: Unknown  
Filed: Herewith Docket: 1133.010US1  
Title: BRYOSTATINS, BRYOPYRANS AND POLYKETIDES: COMPOSITIONS  
AND METHODS  
(Continuation Under 35 U.S.C. 111(a) of PCT/US00/21326,  
filed 04 August 2000)

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**PRELIMINARY AMENDMENT**

Commissioner for Patents  
Washington, D.C. 20231

Prior to examination, please amend the above-identified continuation application as follows:

**In the Specification**

On page 1, after the title, please insert the following:

--This application is a continuation under 35 U.S.C. 111(a) of International Patent Application No. PCT/US00/21326, filed on August 4, 2000, which claims priority from U.S. Provisional Application Serial No. 60/147,283, filed on August 4, 1999, both of which applications are incorporated by reference in their entirety.--

**In the Claims**

Please cancel claims 1-65 without prejudice or disclaimer.

Please add the following new claims 66-89:

66. (New) A composition, comprising: at least one isolated nucleic acid molecule that encodes at least one polypeptide that catalyzes at least one step in the synthesis of at least one polyketide or bryopyran ring, wherein said at least one nucleic acid is derived from at least one marine organism.

67. (New) The composition of claim 66, wherein said at least one bryopyran ring comprises at least one bryostatin.

68. (New) The composition of claim 66, wherein said at least one polypeptide comprises at least one activity of at least one polyketide synthase.

69. (New) The composition of claim 66, wherein said at least one marine organism comprises at least one bacteria or at least one invertebrate.

70. (New) The composition of claim 69, wherein said at least one bacteria comprises at least one *Candidatus*.

71. (New) The composition of claim 70, wherein said at least *Candidatus* comprises at least one *Endobugula*.

72. (New) The composition of claim 71, wherein said at least one *Endobugula* comprises at least one *Endobugula sertula*.

73. (New) The composition of claim 69, wherein said at least one invertebrate comprises at least one *Bugula*.

74. (New) The composition of claim 73, wherein said at least one *Bugula* is *Bugula neritina*, or *Bugula pacifica*.

75. (New) A composition, comprising: at least one isolated polypeptide that catalyzes at least one step in the synthesis of at least one polyketide or bryopyran ring, wherein said at least one polypeptide is derived from at least one marine organism.

76. (New) The composition of claim 75, wherein said at least one bryopyran ring comprises at least one bryostatin.

77. (New) The composition of claim 75, wherein said at least one polypeptide comprises at least one activity of at least one polyketide synthase.

78. (New) The composition of claim 75, wherein said at least one marine organism comprises at least one bacteria or at least one invertebrate.

79. (New) The composition of claim 78, wherein said at least one bacteria comprises at least one Candidatus.

80. (New) A method of making a polyketide or bryopyran ring containing composition, comprising: providing the composition of claim 76, and synthesizing a composition therewith which comprises at least one polyketide or bryopyran ring.

81. (New) A composition made by the method of claim 80.

82. (New) The composition of claim 81, wherein said composition does not comprise a known bryostatin.

83. (New) The composition of claim 81, comprising at least one pharmaceutically acceptable carrier.

84. (New) The composition of claim 81, wherein said composition is a pharmaceutical composition.

85. (New) A method for identifying at least one nucleic acid molecule encoding at least one activity of a PKS, comprising: contacting a nucleic acid molecule of claim 1 with a sample, and identifying nucleic acid molecules in said sample that hybridize with said nucleic acid molecule of claim 66.

86. (New) The composition of claim 66 which hybridizes under moderate hybridization conditions to any one of SEQ ID NOS. 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 30, 31, 32, 33, 34, 35, 36, 37, or the complement thereof.

87. (New) The composition of claim 66 which hybridizes under stringent hybridization conditions to any one of SEQ ID NOS. 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 30, 31, 32, 33, 34, 35, 36, 37, or the complement thereof.

88. (New) An isolated nucleic acid molecule comprising any one of SEQ ID NOS. 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 30, 31, 32, 33, 34, 35, 36, 37, or the complement thereof.

89. (New) An isolated nucleic acid molecule encoding SEQ ID NOS. 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, or 38.

**Remarks**

The specification is amended to add a cross-reference to prior applications. The claims are amended for clarity.

The Examiner is invited to contact the Applicants' Representatives at the below-listed telephone number if there are any questions regarding this communication.

Respectfully submitted,

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